

WHAT IS CLAIMED IS:

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1. A method for achieving a therapeutic effect in a mammal in need thereof which comprises administering to said mammal amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent.

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2. The method according to Claim 1 wherein an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent are administered simultaneously.

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3. The method according to Claim 1 wherein an amount of an antineoplastic agent and an amount of a prenyl-protein transferase inhibitor are administered consecutively.

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4. The method according to Claim 1 wherein the therapeutic effect is treatment of cancer.

5. The method according to Claim 4 wherein the therapeutic effect is selected from inhibition of cancerous tumor growth and regression of cancerous tumors.

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6. The method according to Claim 4 wherein the antineoplastic agent is selected from:

- a) a microtubule-stabilising agent;
- b) a microtubule-disruptor agent;
- c) an alkylating agent;
- d) an anti-metabolite;
- e) epidophyllotoxin;
- f) an antineoplastic enzyme;
- g) a topoisomerase inhibitor;

- h) procarbazine;
- i) mitoxantrone;
- j) a platinum coordination complexe;
- k) a biological response modifier;
- 5 l) a growth inhibitor;
- m) a hormonal/antihormonal therapeutic agent and
- n) a haematopoietic growth factor.

7. The method according to Claim 4 wherein the
10 antineoplastic agent is a member of a class of anti-neoplastic agents, said
class selected from: the anthracycline family of drugs, the vinca drugs,
the mitomycins, the bleomycins, the cytotoxic nucleosides, the taxanes,
the epothilones, discodermolide, the pteridine family of drugs, diynenes,
aromatase inhibitors and the podophyllotoxins.

15 8. The method according to Claim 4 wherein the
antineoplastic agent is selected from: paclitaxel, docetaxel, epothilone A,
epothilone B, desoxyepothilone A, desoxyepothilone B, doxorubicin,
carminomycin, daunorubicin, aminopterin, methotrexate, methopterin,
20 dichloro-methotrexate, mitomycin C, porfiromycin, 5-fluorouracil, 6-
mercaptopurine, gemcitabine, cytosine arabinoside, podophyllotoxin,
etoposide, etoposide phosphate, teniposide, melphalan, vinblastine,
vincristine, leurosidine, vindesine, leurosine, estramustine, cisplatin,
carboplatin, cyclophosphamide, bleomycin, tamoxifen, ifosamide,
25 melphalan, hexamethyl melamine, thiotapec, cytarabin, idatrexate,
trimetrexate, dacarbazine, L-asparaginase, camptothecin, CPT-11,
topotecan, ara-C, bicalutamide, flutamide, leuprolide, a
pyridobenzoindole derivative, an interferon and an interleukin.

30 9. The method according to Claim 4 wherein the
30/27 antineoplastic agent is selected from: paclitaxel, epothilone A, epothilone
B, desoxyepothilone A, desoxyepothilone B, doxorubicin, daunorubicin,
5-fluorouracil, etoposide, vinblastine, estramustine, cisplatin, ara-C and
bicalutamide.

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10. The method according to Claim 4 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine;

1-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

10 2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine;

1-[5-(1-Benzylimidazol)methyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;

15 1-{5-[1-(4-nitrobenzyl)]imidazolylmethyl}-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

20 2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine;

2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

25 2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine;

1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine;

30 1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]acetyl]-4-(1-naphthoyl)piperazine;

2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl]ethyl]-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-3-hydroxypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-piperazine;

2(S)-n-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolylmethyl)-piperazin-5-one;

2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)piperazin-5-one;

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)-
2(S)-(2-methoxyethyl)piperazin-5-one;

5 2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-
ylmethyl]-piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-
ylmethyl]-piperazine;

10 2(S)-*n*-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)piperazine;

15 2(S)-*n*-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)piperazine;

20 2(S)-*n*-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)piperazine;

25 2(S)-*n*-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)piperazine;

30 2(S)-*n*-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)piperazine;

2(S)-*n*-Butyl-1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-*n*-butyl-4-(1-
naphthoyl)piperazine;

2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-
5-ylmethyl]-piperazine;

30 2(S)-*n*-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-
naphthoyl)-piperazine;

2(S)-*n*-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)-piperazine;

5 1-[1-(4-Phenylbenzyl)imidazol-5-ylmethyl]-2(S)-*n*-butyl-4-(1-naphthoyl)-piperazine;

10 2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]-piperazine;

15 2(S)-*n*-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5-ylmethyl]piperazine;

20 1-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}-2(S)-*n*-butyl-4-(1-naphthoyl)piperazine;

25 (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;

30 (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

35 (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;

(\pm)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;

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4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-(imidazolylmethyl)-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)piperazin-2-one;

5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-1-(2-methylphenyl)piperazin-2-one;

4-[1-(4-Cyanobenzyl)-5-imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one;

4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)-piperazin-2-one;

4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one;

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-4-pentenoyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-4-pentenoyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-pentanoyl-homoserine lactone,

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2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy]pentanoyl-homoserine,

5 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]5-pentyloxy-4-methylpentanoyl-homoserine lactone,

10 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-4-methylpentanoyl-homoserine,

15 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-methylbutanoyl-homoserine lactone,

20 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylbutanoyl-homoserine lactone,

25 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

30 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine lactone,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoserine,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy]pentanoyl-homoserine,

Part 2
cont

5 pentyloxy-3-phenylpropionyl-methionine/methyl ester,

2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine,

10 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone methyl ester,

15 2(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester,

20 2-(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone methyl ester,

25 2-(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone methyl ester,

30 2-(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone,

2-(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-methybutanoyl-methionine methyl ester.

2-(S)-[2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-methybutanoyl-methionine,

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Disulphide of 2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

5 Disulphide of 2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,

Disulphide of 2(S)-[2(R)-Amino-3-mercaptopropylamino-3(S)methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester

10 1-(4-Biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-5-(4'-phenylbenzamido)ethyl-imidazole

15 1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Biphenylethyl)-5-(4-cyanobenzyl)imidazole

20 1-(2'-Bromo-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

25 1-(2'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

30 1-(4-(3',5'-dichloro)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

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1-(2'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

5 1-(2-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

10 1-(3-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

15 1-(4-(3',5'-Bis-trifluoromethyl)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

20 1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)-4-methylimidazole

25 1-(4-Biphenylmethyl)-5-(4-cyanophenoxy)-imidazole

30 5-(4-Cyanophenoxy)-1-(2'-methyl-4-biphenylmethyl)-imidazole

35 5-(4-Biphenyloxy)-1-(4-cyanobenzyl)-imidazole

5-(2'-Methyl-4-biphenyloxy)-1-(4-cyanobenzyl)-imidazole

30 5-(4-(3',5'-dichloro)biphenylmethyl)-1-(4-cyanobenzyl)imidazole

35 1-(4-biphenylmethyl)-5-(1-(R,S)-acetoxy-1-(4-cyanophenyl)methyl)imidazole

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1-(4-Biphenylmethyl)-5-(1-(R,S)-hydroxy-1-(4-cyanophenyl)methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-amino-1-(4-cyanophenyl)methylimidazole

10 1-(4-biphenylmethyl)-5-(1-(R,S)-methoxy-1-(4-cyanophenyl)methylimidazole

15 1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-oxo-1-(4-biphenyl)-methyl imidazole

20 1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-fluoro-4-biphenyl)-methyl)-imidazole

25 1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-biphenyl)methyl-imidazole

30 5-(2-[1,1'-Biphenyl]vinylene)-1-(4-cyanobenzyl)imidazole

35 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

1-(4-Biphenylmethyl)-5-(4-bromophenoxy)-imidazole

1-(3'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

*Sub A2
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1-(4'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

10 1-(4'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

15 1-(4'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

20 1-(2'3'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'4'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

25 1-(2'5'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

30 1-(3'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

cont 1-(4-(2'-Trifluoromethylphenyl)-2-Chlorophenylmethyl)-5-(4-cyanobenzyl) imidazole

5 1-{1-(4-(2'-trifluoromethylphenyl)phenyl)ethyl}-5-(4-cyanobenzyl) imidazole

10 1-(2'-Trifluoromethyl-4-biphenylpropyl)-5-(4-cyanobenzyl) imidazole

15 1-(2'-N-t-Butoxycarbonylamino-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

20 1-(2'-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

25 1-(2'-Acetylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

30 1-(2'-Methylsulfonylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Ethylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

25 1-(2'-Phenylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

30 1-(2'-Glycinylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)-2-chloro-5-(4-cyanobenzyl) imidazole

*Sub 2
cont*

1-(2'-Methyl-4-biphenylmethyl)-4-chloro 5-(4-cyanobenzyl)imidazole

5 1-(3'-Chloro-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl)imidazole

10 1-(3'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

15 1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl)imidazole

20 1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

25 1-(3'-Methoxy-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

30 1-(2'-Chloro-4'-fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

35 1-(2'-(2-Propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-(2-Methyl-2-propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(2'-Ethyl-4-biphenylmethyl)-5-(4-(1*H*-tetrazol-5-yl))benzyl)imidazole

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethoxy]-4-(2'-methylphenyl)-2-(3-N-phthalimido-1-propyl)benzene

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1-(3',5'-Ditrifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(3',5'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(3',5'-Dimethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

25

1-(3-(N-Boc-aminomethyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(3-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(4-Cyanobenzyl)-2-methyl-5-(2'-methylbiphenyl-4-yloxy)imidazole

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5-(4-Cyanobenzyl)-1-(3-cyano-2'-trifluoromethylbiphenyl-4-ylmethyl)-imidazole

5 2-Amino-5-(biphenyl-4-ylmethyl)-1-(4-cyanobenzyl)imidazole

2-Amino-1-(biphenyl-4-ylmethyl)-5-(4-cyanobenzyl)imidazole

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1-(3-Butylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

15 1-(3-Propylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole

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1-(4-Biphenylmethyl)-4-(4-cyanobenzyl)-2-methylimidazole

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1-(4-Cyanobenzyl)-5-[3-fluoro-4-biphenyl)methyl]imidazole

25 1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)-1-hydroxy]ethyl-2-methylimidazole

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1-(4-Cyanobenzyl)-5-(4-biphenylmethyl)-2-methylimidazole

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1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]ethyl-2-methyl imidazole

35 1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]vinylidene-2-methylimidazole
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1-(4-Cyanobenzyl)-5-[2-(4-biphenyl)]vinylene-2-methylimidazole

1-(4-[Pyrid-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-[3-Methylpyrazin-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

10 1-(4-(Pyrimidinyl-5-yl)phenylmethyl)-5-(4-cyanobenzyl)imidazole

15 1-(2-Phenylpyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

15 1-(2-Phenyl-N-Oxopyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-N-Oxopyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

20 1-(2-(3-Trifluoromethoxyphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

25 1-(2-(2-Trifluoromethylphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-2-Chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-4-chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

30 1-(2-Amino-3-phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-[Pyrid-2-yl]pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

35 N-{1-(4-Cyanobenzyl)-1H-imidazol-5-yl)methyl}-5-(pyrid-2-yl)-2-amino-pyrimidine

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carbomethoxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carbomethoxyphenyl)oxy]benzene

10 *N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3-carboxyphenyl)oxy]benzene*

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3-carbomethoxyphenyl)oxy]benzene

15 *N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-3-(phenoxy)benzene*

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenoxy)benzene

20 *N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenylthio)benzene*

N-Butyl-N-[1-(4-cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

25 *N-[1-(4-Cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene*

N-(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

30 *1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene*

(±)-4-[(4-imidazolylmethyl)amino]pentyl-1-(phenoxy)benzene

35 *1-[(N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino)methyl]-4-(phenoxy)benzene*

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4-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylthio)benzene

(\pm)-4-[N-(1-(4-cyanobenzyl)-4-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylsulfinyl)benzene

3-[N-(4-imidazolylmethyl)-N-(n-butyl)amino]-N-(phenyl)benzenesulfonamide and

10 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

15 4-{3-[4-(2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

20 4-{3-[4-3-Methyl-2-oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

25 4-{3-[4-(2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl}benzonitrile

(4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl})-benzonitrile

30 4-{3-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile

4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3H-imidazol-4-ylmethyl}-benzonitrile

35 4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}-benzonitrile

Jahr
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cont

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4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile

4-[3-(2-Oxo-1-phenyl-1,2-dihdropyridin-4-ylmethyl)-3H-imidazol-4-ylmethyl]benzonitrile

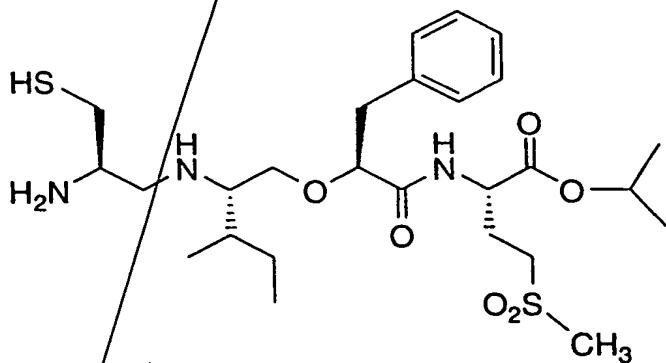
10 4-{3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihdropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl}benzonitrile

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

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11. The method according to Claim 4 wherein the prenyl-protein transferase inhibitor is selected from:

20 2(S)-[2(S)-[2(R)-Amino-3-mercaptop]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



25 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

12 cont
 (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

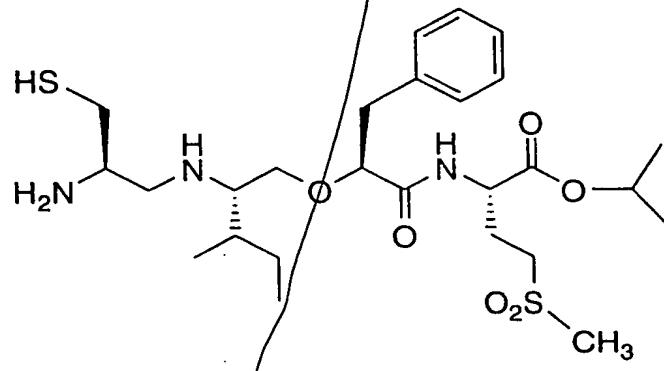
4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

10 or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

12. The method according to Claim 4 wherein the antineoplastic agent is paclitaxel and the prenyl-protein transferase 15 inhibitor is

2(S)-[2(S)-[2(R)-Amino-3-mercaptopo]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



20 13. A method of treating cancer in a mammal in need thereof which comprises administering to said mammal amounts of a prenyl-protein transferase inhibitor and applying to the mammal radiation therapy.

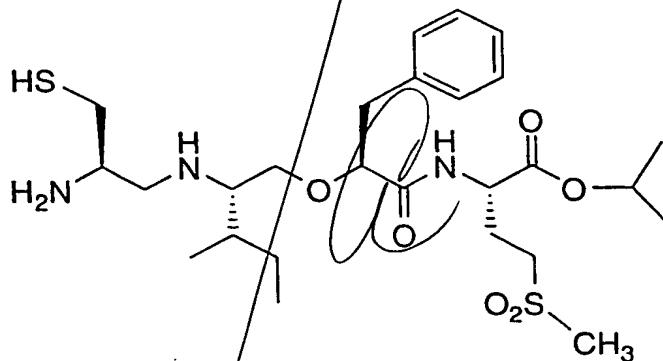
14. The method according to Claim 13 wherein the amount of a prenyl-protein transferase inhibitor and the radiation therapy are administered simultaneously.

5 15. The method according to Claim 13 wherein the amount of a prenyl-protein transferase inhibitor is administered first and the radiation therapy is administered after the prenyl-protein transferase inhibitor has been administered.

10 16. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-[2(S)-[2(R)-Amino-3-mercaptop]-propylamino-
3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone

15 isopropyl ester (Compound A)



1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

20 (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

25 4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

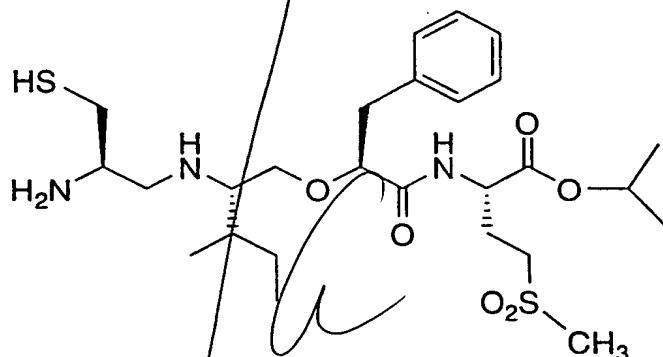
1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

or a pharmaceutically acceptable salt, disulfide or optical isomer

5 thereof.

17. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is selected from:

10 2(S)-[2(S)-[2(R)-Amino-3-mercaptop]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



15 or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

18. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is:

20 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

or a pharmaceutically acceptable salt thereof.

25

19. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is selected from:

5 (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

or a pharmaceutically acceptable salt or optical isomer thereof.

10 20. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is selected from:

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

15 or a pharmaceutically acceptable salt thereof.

21. The method according to Claim 13 wherein the prenyl-protein transferase inhibitor is selected from:

20 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

or a pharmaceutically acceptable salt thereof.

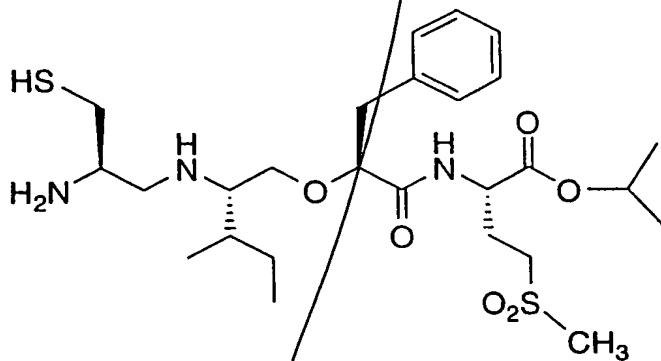
25 22. The method according to Claim 13 which additionally comprises administering to the mammal an amount of an antineoplastic agent.

30 23. The method according to Claim 22 wherein the amount of a prenyl-protein transferase inhibitor and the amount of an antineoplastic agent are administered simultaneously.

35 24. The method according to Claim 22 wherein the amount of an antineoplastic agent and the amount of a prenyl-protein transferase inhibitor are administered consecutively.

25. The method according to Claim 22 wherein the prenyl-protein transferase inhibitor is selected from:

5 2(S)-[2(R)-Amino-3-mercaptop]-propylamino-3(S)-methyl-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



10 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;
(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;

15 4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

20 1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene
or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

25 26. A pharmaceutical composition for achieving a therapeutic effect in a mammal in need thereof which comprises

amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent

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Sub A3 27. The pharmaceutical composition according to Claim 26 comprising an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent.

10

28. The pharmaceutical composition according to Claim 26 wherein the therapeutic effect is treatment of cancer.

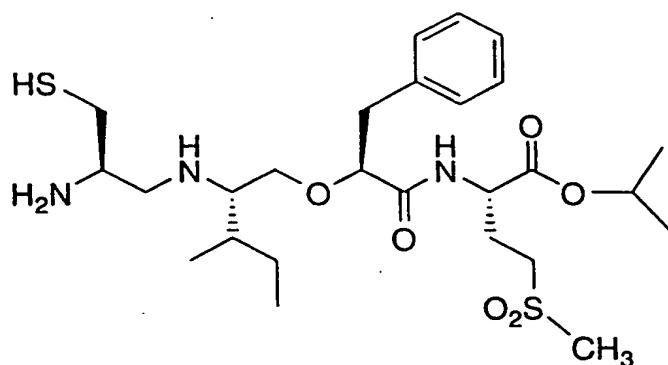
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29. The pharmaceutical composition according to Claim 26 wherein the therapeutic effect is selected from inhibition of cancerous tumor growth and the regression of cancerous tumors.

20

30. The composition according to Claim 27 wherein the antineoplastic agent is paclitaxel and the prenyl-protein transferase inhibitor is

2(S)-[2(S)-[2(R)-Amino-3-mercaptop]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)



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31. A method of preparing a pharmaceutical composition for achieving a therapeutic effect in a mammal in need thereof which

*sub
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cont*) comprises mixing amounts of at least two therapeutic agents selected from a group consisting of:

5 a) a prenyl-protein transferase inhibitor and
 b) an antineoplastic agent.

32. The method of preparing a pharmaceutical composition according to Claim 26 comprising mixing an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent.

Add A'7
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